DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for obesity and Type II diabetes, does not reasonably provide enablement for type I diabetes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Pursuant to ***In re Wands***, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see ***In re Vaeck***, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims. The claims cover a limited number of species. The remarks state that the scope is "not unreasonably broad". The examiner is not saying that it is. Applicants are not just claiming a single species. Breadth of claims is just one of several factors which must be taken into account.

(2) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See ***In re Fisher***, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The remarks brush off the ***Fischer*** case as being "nearly 40 years old." ***In re Fisher*** is not considered to be outdated caselaw. It is cited in MPEP 2164.03; and was cited in ***Monsanto Co. v. Syngenta Seeds Inc.***, 84 USPQ2d 1705 (Fed. Cir. 2007); ***In re Wright***, 27 USPQ2d 1510 (Fed. Cir. 1993); ***Ex parte Primakoff***, 64 USPQ2d 1848 and ***Ex parte Varshavsky***, 63 USPQ2d 1486 (2001).

(3) Direction or Guidance: That provided is very limited. The dosage range information on page 27 is a 120 fold range, and does not take into account the weight of subject (normally, dosages are given in mg/kg). Moreover, this is generic, the same for the many disorders covered by the specification. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for type I diabetes. The remarks state that "dosing of the compounds within the does range would be routine to one of ordinary skill in the art." This statement is not agreed with. First, as noted, the dosage information is defective, as it does not take into account body weight. Second, how can this be "routine" if no inhibitors of

DPP-IV (or inhibitors of anything else for that matter) have ever been used for the treatment of type-1 diabetes?

(4) State of the Prior Art: These compounds are xanthines with a particular substitution pattern at the 7- and 8-positions. So far as the examiner is aware, no xanthines of any kind have been used for the treatment or prevention of type I diabetes.

(5) Working Examples: There are none for the treatment of any disease. There is a test showing that these compounds are inhibitors of DPP-IV, but this is not a standard test for any of these utilities. Applicants state, "Regarding working examples, it is not required that applicants provide working examples of the actual method." The examiner has not said that working examples are required; this is just one of many factors to be considered. As was stated in ***Ex parte Sudilovsky***, 21 USPQ2d 1702: "Though not controlling, the lack of working examples, is, nevertheless, a factor to be considered in a case involving both physiological activity and an undeveloped art. When a patent applicant chooses to forego exemplification and bases utility on broad terminology and general allegations, he runs the risk that unless one with ordinary skill in the art would accept the allegations as obviously valid and correct, the examiner may, properly, ask for evidence to substantiate them. ***In re Novak***, 306 F.2d 924, 134 USPA 335 (CCPA 1962) 4; ***In re Fouche***, 439 F.2d 1237, 169 USPQ 429 (CCPA 1971)." This is particularly true in the current situation, where no DPPIV inhibitor --- or indeed, any other enzyme inhibitor --- has ever been show effective for the treatment of type-1 diabetes. Thus, while applicants state, "The showing of DPP IV inhibition effect is sufficient guidance to provide a reasonable expectation of success in view of the connection between DPP IV inhibition and type 1 diabetes treatment", applicants are

referring to a connection to "type 1 diabetes treatment" that simply does not exist. There is no established "type 1 diabetes treatment" arising from DPP IV inhibition.

(6) Skill of those in the art: Type I Diabetes treatment, what little there is, tends to be via immune suppressants, since this is an auto-immune disorder. The skill level for the treatment for Type I diabetes is exceptionally low. Type 1 diabetes is an autoimmune disease that results in the irreversible destruction of insulin producing beta cells of the Langerhans islets in the pancreas. Despite the urgent need --- Type I diabetes is lethal unless the insulin is somehow replaced --- no pharmaceutical has ever been found effective against this disorder. Diet and exercise cannot reverse or prevent type 1 diabetes, although these are important in regulating the insulin given to the patient. Patients are treated either with insulin replacement therapy, or with transplantation surgery, either islet cell transplantation or, less commonly, pancreas transplantation. These do not treat the disorder per se, but only shield the patient from the lethal consequences. Patients may be given drugs for e.g. nephropathy or poor blood circulation in the feet, but these do not treat the disease itself, only the consequences of the lack of insulin. Applicants state, "The level of one of ordinary skill in the art for this art would be at a high level and, thus, supports a finding of enablement. One skilled in this art, e.g., an endocrinologist, would be highly educated, i.e., Ph.D. level, and very familiar with the treatment and pathology of type 1 diabetes." That refers to the skill level of the people who do medical treatment. That is always high. The question here is the skill level in the particular art itself, which is the treatment of type-1 diabetes with DPP-IV inhibitors, or, more broadly, the treatment of type-1 diabetes with anything at all. The skill level on that area is low, as is evidenced by the woeful lack of success.

The compounds claimed here are DPP-IV inhibitors. Applicants have cited the Pospisilik reference, which applicants assert as providing evidence "showing a connection between DPP IV inhibitor effect and treatment of type 1 diabetes." Actually, that overstates what the reference has, as treatment of type 1 diabetes was never even attempted. Instead, it notes promising results in an animal model. This model, however, is not recognized as being a reliable predictor for drugs which are effects against Type 1 diabetes, nor could it, since here are at present no such drugs. Indeed, while Type 1 diabetes in humans is an autoimmune disorder, the rats involved have no autoimmune disorder, but instead were treated with a toxin. Further, the reference does not even imply that this kind of treatment constitutes enablement, but to the contrary, it says that "The findings set the foundation for additional study into the application of DP IV inhibitors in the treatment of insulin-dependent diabetes (type 1 and late-stage type 2)..." The research thus does not show that the compounds would be expected to be useful but instead, the research sets "the foundation for additional study". The statement that "additional study" is needed is a clear indication that enablement is not present.

Further, to rebut this notion that such a DPP-IV inhibitor is suitable for type-1 diabetes, the examiner notes that there is a DPP-IV inhibitor on the market, called Januvia™ (sitaglipin). Specific product information on this drug states explicitly that it is not to be used with patients having Type 1 diabetes. The reference "Patient Information JANUVIA™ " which applicants have provided is presented as an example. This is in fact explicit evidence that not only is treatment of type-1 diabetes with DPP-IV inhibitors not enabled, it is actually contraindicated.

(7) The quantity of experimentation needed: Owing especially to factors 3, 4, 5 and 6, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. ***In re Wright***, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Mark L. Berch/ whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone numbers for

the organization where this application or proceeding is assigned are (571) 273-8300 for regular communications and (571) 273-8300 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.

/Mark L. Berch/
Primary Examiner
Art Unit 1624

6/16/2008